EXHIBIT "C"

1: J Biol Chem. 1998 Oct 2;273(40):25545-7.

Reversibility of scrapie inactivation is enhanced by copper.

McKenzie D, Bartz J, Mirwald J, Olander D, Marsh R, Aiken J.

Department of Animal Health and Biomedical Sciences, University of Wisconsin-Madison, Madison, Wisconsin 53706, USA. mckenzie@ahabs.wisc.edu

The only known difference between the cellular (PrPC) and scrapie-specific (PrPSc) isoforms of the prion protein is conformational. Because disruption of PrPSc structure decreases scrapie infectivity, restoration of the disease-specific conformation should restore infectivity. In this study, disruption of PrPSc (as monitored by the loss of proteinase K resistance) by guanidine hydrochloride (GdnHCl) resulted in decreased infectivity. Upon dilution of the GdnHCl, protease resistance of PrP was restored and infectivity was regained. The addition of copper facilitated restoration of both infectivity and protease resistance of PrP in a subset of samples that did not renature by the simple dilution of the GdnHCl. These data demonstrate that loss of scrapie infectivity can be a reversible process and that copper can enhance this restoration of proteinase K resistance and infectivity.

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